Clonal isolation of endothelial colony-forming cells from early gestation chorionic villi of human placenta for fetal tissue regeneration.

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Authors: Kewa Gao, Siqi He, Priyadarsini Kumar, Diana Farmer, Jianda Zhou, Aijun Wang

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Public Summary:
Endothelial colony-forming cells are involved in the process of vascularization including vasculogensesis and angiogenesis. Vasculogenesis is the new formation of blood vessels which occurs during embryonic development and tissue regeneration. Angiogenesis is the growth of new capillaries from pre-existing blood vessels, which is observed both prenatally and postnatally. The placenta is an organ composed of a variety of fetal-derived cells, including endothelial colony-forming cells, and therefore has significant potential as a source of fetal endothelial colony-forming cells for tissue engineering. Our goal is to investigate the possibility of isolating clonal endothelial colony-forming cells from human early gestation chorionic villi of the placenta, and assess their potential for tissue engineering.

Scientific Abstract:
BACKGROUND: Endothelial colony-forming cells (ECFCs) have been implicated in the process of vascularization, which includes vasculogenesis and angiogenesis. Vasculogenesis is a de novo formation of blood vessels, and is an essential physiological process that occurs during embryonic development and tissue regeneration. Angiogenesis is the growth of new capillaries from pre-existing blood vessels, which is observed both prenatally and postnatally. The placenta is an organ composed of a variety of fetal-derived cells, including ECFCs, and therefore has significant potential as a source of fetal ECFCs for tissue engineering. AIM: To investigate the possibility of isolating clonal ECFCs from human early gestation chorionic villi (CV-ECFCs) of the placenta, and assess their potential for tissue engineering. METHODS: The early gestation chorionic villus tissue was dissociated by enzyme digestion. Cells expressing CD31 were selected using magnetic-activated cell sorting, and plated in endothelial-specific growth medium. After 2-3 wks in culture, colonies displaying cobblestone-like morphology were manually picked using cloning cylinders. We characterized CV-ECFCs by flow cytometry, immunophenotyping, tube formation assay, and Dil-Ac-LDL uptake assay. Viral transduction of CV-ECFCs was performed using a Luciferase/tdTomato-containing lentiviral vector, and transduction efficiency was tested by fluorescent microscopy and flow cytometry. Compatibility of CV-ECFCs with a delivery vehicle was determined using an FDA approved, small intestinal submucosa extracellular matrix scaffold. RESULTS: After four passages in 6-8 wks of culture, we obtained a total number of 1.8 x 10(7) CV-ECFCs using 100 mg of early gestational chorionic villus tissue. Immunophenotypic analyses by flow cytometry demonstrated that CV-ECFCs highly expressed the endothelial markers CD31, CD144, CD146, CD105, CD309, only partially expressed CD34, and did not express CD45 and CD90. CV-ECFCs were capable of acetylated low-density lipoprotein uptake and tube formation, similar to cord blood-derived ECFCs (CB-ECFCs). CV-ECFCs can be transduced with a Luciferase/tdTomato-containing lentiviral vector at a transduction efficiency of 85.1%. Seeding CV-ECFCs on a small intestinal submucosa extracellular matrix scaffold confirmed that CV-ECFCs were compatible with the biomaterial scaffold. CONCLUSION: In summary, we established a magnetic sorting-assisted clonal isolation approach to derive CV-ECFCs. A substantial number of CV-ECFCs can be obtained within a short time frame, representing a promising novel source of ECFCs for fetal treatments.